A2 cont.

consisting of buccal, endotracheal, inhalation, nasal, pharyngeal, rectal, sublingual and vaginal.

REMARKS

The instant invention is drawn *inter alia* to methods of treating and preventing arthritis using androstenediones.

Claims 12-21 have been cancelled without prejudice to future prosecution.

Claims 1-11 have been amended to facilitate prosecution of the instant invention. Attached hereto is a marked up version of the changes made to these claims by the instant Amendment captioned "Version with Markings to Show Changes Made". The amendments to the claims are fully supported by the specification and claims as filed and add no new matter. The majority of the amendments modify the form of the claim language unrelated to patentability. Independent claim 1 was modified to delete the term "appreciably" as well.

New claims 22-38 have been added to more completely encompass the instant invention. The new claims are fully supported by the specification and claims as filed and add no new matter. Support for new claim 22 can be found on page 1, lines 14-19 and page 2, lines 30-31. Support for new claims 23-30 can be found, for example, in the claims as originally filed. Support for new claims 31, 32, 37 and 38 can be found, for example, on page 5, line 18 through page 6, line 13. Support for new claims 33-36 can be found on page 2, lines 23-24, for example.

In general, the scope of the claimed subject matter has not been altered or has been increased.

ARGUMENTS

Claim Rejections - 35 U.S.C. § 112, First Paragraph

Claims 1, 3-12 and 14-21 stand rejected under 35 U.S.C. § 112, first paragraph for alleged lack of enablement. The

Examiner alleges that metabolizable precursors of Δ5-androstene-3β-ol-7,17-dione that are incapable of being appreciably metabolized to androgens, estrogens or DHEA are not enabled. Applicant respectfully traverses this rejection as it applies to the claims as amended.

Claims 12 and 14-21 have been cancelled rendering this rejection moot. Independent claim 1, from which claims 3-11 depend, has been amended to delete the phrase "metabolizable precursors" and to include the phrase "3β esters thereof". The group of compounds that is encompassed by 3β esters of Δ5-androstene-3β-ol-7,17-dione is easily identifiable by those of ordinary skill in the art. In addition, an example of what is meant is provided by Δ5-androstene-3β-acetoxy-7,17-dione described therein.

Based on the above, Applicant respectfully requests that the rejection of currently pending claims 1-11 under 35 U.S.C. § 112, first paragraph be withdrawn.

Claim 3:

The Examiner states that claim 3 allegedly fails to further limit the base claim. Applicant traverses this rejection as it applies to the claims as amended.

Claim 3 further limits the base claim by specifying that the patient is human. Therefore, Applicant respectfully requests that the rejection of claim 3 under 35 U.S.C. § 112, first paragraph be withdrawn.

Claims 18 & 21:

The Examiner states that claims 18 and 21 are allegedly substantial duplicates to one another. The Examiner alleges that "the method steps in both claims are identical and the patients are the same." Applicant traverses this rejection as it applies to the claims as amended. Claims 18 and 21 have been cancelled rendering this rejection moot.

Therefore, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, first paragraph as it applies to the claims as amended, be withdrawn.

Claim Rejections - 35 U.S.C. § 112, Second Paragraph

Claims 1-21 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. Applicant respectfully traverses this rejection as it applies to the claims as amended.

Claims 1 and 12 - "appreciably metabolized"

The Examiner alleges that the term "appreciably metabolized" renders the claims indefinite as to what steroid compounds are encompassed by the claims. This rejection is traversed as it applies to the claims as amended.

The term "appreciably" has been deleted from claims 1 and 12 rendering this rejection moot. Therefore, Applicants respectfully request that this rejection for alleged indefiniteness under 35 U.S.C. § 112, second paragraph be withdrawn.

Claims 7 and 11-20 - "arthritis-related tissue inflammation"

The Examiner alleges that the term "arthritis-related tissue inflammation" renders the claims indefinite as to what patients are encompassed by the claims. This rejection is traversed as it applies to the claims as amended.

Claims 12 to 20 have been cancelled rendering this rejection moot as to those claims. Claims 7 and 11 have been amended to clarify the claimed invention. They depend from claim 1, where the patients encompassed by the claims are those patients in need of arthritis treatment or prevention. Claims 7 and 11 identify a subset of those patients either afflicted or diagnosed with arthritis-related tissue inflammation.

Claims 12 - "a treatment method...preventative amount"

The Examiner alleges that it is unclear whether the method is for prevention or for treatment. Applicant respectfully traverses this rejection as it applies to the claims as amended. Claim 12 has been cancelled rendering this rejection moot.

In view of the above, Applicant respectfully requests that the rejection under 35 U.S.C. § 112, second paragraph as it applies to the claims as amended, be withdrawn.

Claim Rejections - 35 U.S.C. § 102

Claims 12-13 stand rejected under 35 U.S.C. § 102(b) for alleged anticipation by Lardy (U.S. Patent 5,585,371). The Examiner alleges that "Applicants' failure to distance the proffered claims from the anticipated prophylactic utility, renders such claims anticipated by the prior inherent use." This rejection is traversed as it applies to the claims as amended.

The Examiner cites Ex parte Novitski for the proposition that the instant invention is inherently anticipated by Lardy. However, in Ex parte Novitski a known compound that had previously been used to treat a certain class of subjects (plants) to achieve one effect (protection against fungal disease) was later being used against the same class of subjects (plants) to achieve a different affect (inhibit nematodes). Here, Lardy is arguably administering a known compound (e.g. Δ5-androstene-3β-ol-7,17-dione) to one class of subjects (e.g. those in need of improving antibody responsiveness of the immune system) to achieve one affect (that of improving antibody responsiveness of the immune system. Whereas in the instant application, a known compound (e.g. Δ5-androstene-3β-ol -7,17-dione) is administered to a different class of subjects (those in need of arthritis prevention or treatment) to achieve a different effect (that of preventing or treating arthritis). Unlike in Ex parte Novitski, the classes of subjects in Lardy and in the

instant application are Not the same (those in need of improving antibody responsiveness of the immune system versus those in need of arthritis prevention or treatment). Thus, based on Ex parte Novitski, the instant invention is not inherently anticipated by Lardy.

Therefore, Applicants respectfully request that this rejection for alleged anticipation under 35 U.S.C. § 102 be withdrawn.

Claim Rejections - 35 U.S.C. § 103(a)

Claims 1-11 and 14-21 stand rejected under 35 U.S.C. § 103(a) for alleged obviousness over Lardy in view of Peat (U.S. Patent 4,628,052). This rejection is respectfully traversed as it applies to the claims as amended.

As stated previously, Lardy is drawn, *inter alia*, to the use of Δ5-androstene-3β-ol-7,17-dione to improve antibody responsiveness of the immune system. Peat describes the use of DHEA for arthritis. The Examiner alleges that the motivation to combine arises from Lardy allegedly teaching that Δ5-androstene-3β-ol-7,17-dione and DHEA "have a similar immunological effect" and Peat teaching that DHEA is useful in treating arthritis.

In fact, Lardy provides objective evidence that DHEA and Δ5-androstene-3β-ol-7,17-dione do NOT have a similar immunological effect by stating under "Conclusions" (column 10, lines 31-33), "Δ5-androstene-3β-ol-7,17-dione is also substantially **superior** to DHEA in enhancement of immune system response" (Emphasis added). A compound that acts in a superior manner to another compound does not have a similar immunological effect and so this motivation to combine fails.

The instant specification provides additional evidence that DHEA and Δ5-androstene-3β-ol-7,17-dione differ in their "pharmacological activities" by stating in the "Detailed Description of the Invention" (page 4, lines 28-30), "Δ5-

androstene-3β-ol-7,17-dione is a derivative of dehydroepiandrosterone (DHEA) which does not appreciably stimulate, increase or otherwise enhance the production of sex hormones." This is stated as a contrast to DHEA. The lack of stimulation of sex hormones in combination with the superiority of immune enhancement, strongly support the argument that DHEA and Δ5-androstene-3β-ol-7,17-dione do NOT have the same pharmacological effects. Thus, the activity of DHEA against arthritis would NOT indicate to one of ordinary skill in the art that Δ5-androstene-3β-ol-7,17-dione would be active against arthritis.

Finally, Lardy teaches away from the instant invention. Lardy teaches, *inter alia*, the use of Δ5-androstene-3β-ol-7,17-dione to enhance immune function and in particular to improve the immune response to an antigen. Arthritis is a disorder with inflammatory components. As stated in the specification, it is typically treated with anti-inflammatory drugs (page 2, lines 4-9 describing conventional treatment for osteoarthritis; page 2, lines 17-18 describing conventional treatment for fibromyalgia; and page 3, lines 8-14 describing conventional treatment for rheumatoid arthritis). Further, rheumatoid arthritis has an autoimmune aspect "generally characterized by inflammation of the membrane lining the joint resulting from an attack upon the joint by the body's own immune system" (page 2, lines 22-23). Accordingly, based on Lardy one of ordinary skill in the art would expect that administration of Δ5-androstene-3β-ol-7,17-dione (an immune enhancer) would exacerbate, rather than treat, arthritis. Such a teaching away from the claimed invention is a significant factor to be considered in determining obviousness and cannot be ignored.

In view of the above, Applicant respectfully requests that the obviousness rejection under 35 U.S.C. § 103(a) be withdrawn.

SUMMARY

Applicants assert that the claimed invention is in condition for allowance and notification to that effect is respectfully requested.

Any fees due in relation to the timely filing of this Response are hereby authorized to be deducted from Deposit Account No. 501536.

Respectfully submitted,

Date: April 3, 2002

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A [treatment] method of treating or preventing arthritis in a patient in need of such treatment or prevention, comprising [treating an arthritis affected] administering to said patient [in need of such treatment with an effective tissue inflammation ameliorative amount of] a steroid selected from the group consisting of Δ5-androstene-3β-ol-7,17-dione and [metabolizable precursors] 3β esters thereof [incapable of being metabolized to androgens, estrogens or dehydroepiandrosterone], wherein said administration results in amelioration or prevention of one or more symptoms of arthritis.

2. (Amended) The [treatment] method of claim 1, wherein [the method comprises treating an arthritis affected patient with an effective amount of a tissue inflammation ameliorative amount of a] said steroid is [selected from Δ5-androstene-3β-ol-7,17-dione and] Δ5-androstene-3β-acetoxy-ol-7,17-dione.

3. (Amended) The [treatment] method of either one of claims 1 [or] and 2 wherein [the method of treating an arthritis affected patient comprises treating an arthritis affected] said patient is human [patient].

4. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating a human] said patient is afflicted with osteoarthritis.

5. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient

comprises treating a human] said patient is afflicted with fibromyalgia.

6. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating a human] said patient is afflicted with rheumatoid arthritis.

7. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating an arthritis affected] said patient is afflicted with arthritis-related tissue inflammation.

8. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating a human] said patient is diagnosed with osteoarthritis.

9. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating a human] said patient is diagnosed with fibromyalgia.

10. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating a human] said patient is diagnosed with rheumatoid arthritis.

11. (Amended) The [treatment] method of claim 3, wherein [the method of treating an arthritis affected human patient comprises treating an arthritis affected] said patient is diagnosed with arthritis-related tissue inflammation.